AMENDMENT TO THE CLAIMS

1-4. **(Canceled)**

5. **(Currently Amended)** An adzyme for enzymatically altering a substrate, the adzyme being a fusion protein comprising: a [[catalytic]] protease domain that cleaves at least one peptide bond of said substrate to produce one or more products, and a polypeptide targeting domain that reversibly binds with an address site on said substrate or with an address site on a second molecule that occurs in functional proximity to the substrate, wherein

wherein said targeting domain and said protease domain are discrete and heterologous with respect to each other,

~~said adzyme is resistant to cleavage by the catalytic domain~~,

said targeting domain, when provided separately, binds to the substrate,

said [[catalytic]] protease domain, when provided separately, cleaves at least one peptide bond of said substrate to produce one or more products, and

~~said adzyme is more potent than said catalytic domain or targeting moiety with respect to the reaction with said substrate~~,

wherein the substrate is a biomolecule in a biomolecular accretion.

6. **(Canceled)**

7. **(Previously Presented)** The adzyme of claim 5, wherein the substrate is endogenous to a human patient.

8. **(Previously Presented)** The adzyme of claim 7, wherein the adzyme is effective against the substrate in the presence of physiological levels of human serum protein.

9. **(Previously Presented)** The adzyme of claim 8, wherein the human serum protein is human serum albumin.

10-25. **(Canceled)**

26. **(Currently Amended)** The adzyme of claim 5 [[25]], wherein said fusion protein includes a linker between said [[catalytic]] protease domain and said targeting domain.

27. **(Previously Presented)** The adzyme of claim 26, wherein said linker is an unstructured peptide.

28. **(Canceled)**

29. **(Original)** The adzyme of claim 27, wherein said linker includes one or more repeats of Ser_4Gly or $SerGly_4$.

30. **(Canceled)**

31. **(Currently Amended)** The adzyme of claim 26, wherein said linker is selected to provide steric geometry between said catalytic domain and said targeting domain such that said adzyme is more active [[potent]] than said catalytic domain or targeting domain with respect to the reaction with said substrate.

32-34. **(Canceled)**

35. **(Currently Amended)** The adzyme of claim 5 [[25]], wherein the fusion protein is a cotranslational fusion protein encoded by a recombinant nucleic acid.

36. **(Canceled)**

37. **(Currently Amended)** The adzyme of claim 5, wherein the ~~substrate is a~~ biomolecule is produced by a cell.

38-47. **(Canceled)**

48. **(Currently Amended)** The adzyme of claim 5 [[47]], wherein the biomolecular accretion is selected from among: an amyloid deposit and an atherosclerotic plaque.

49. **(Currently Amended)** The adzyme of claim 5 [[37]], wherein the biomolecular accretion is ~~biomolecule is a biomolecule~~ produced by a pathogen.

50. **(Currently Amended)** The adzyme of claim 49, wherein the pathogen is ~~selected from among,~~ a protozoan, a fungus, a bacterium, or [[and]] a virus.

51. **(Currently Amended)** The adzyme of claim 5 [[37]], wherein the biomolecular accretion comprises ~~biomolecule is~~ a prion protein.

52-55. **(Canceled)**

56. **(Withdrawn, Currently Amended)** The adzyme of claim 5 [[52]], wherein said protease is a zymogen.

57. **(Canceled)**

58. **(Currently Amended)** The adzyme of claim 5 [[52]], wherein said adzyme is purified from a cell culture in the presence of a reversible protease inhibitor.

59-68. **(Canceled)**

69. **(Currently Amended)** The adzyme of claim 5, wherein the adzyme is resistant to cleavage by the [[catalytic]] protease domain at an adzyme concentration that is about equal to the concentration of adzyme in a solution to be administered to a subject.

70. **(Currently Amended)** The adzyme of claim 5 [[37]], wherein said adzyme alters the half-life of the biomolecule *in vivo*.

71. **(Canceled)**

72. **(Currently Amended)** The adzyme of claim 5 [[37]], wherein said adzyme alters the distribution of the biomolecule *in vivo*.

73. **(Canceled)**

74. **(Currently Amended)** The adzyme of claim 5 [[37]], wherein said adzyme reduces a biological activity of said biomolecule.

75. **(Canceled)**

76. **(Currently Amended)** The adzyme of claim 5 [[37]], wherein said biomolecule binds a plurality of different molecules *in vivo*, and said adzyme alters the binding specificity of said biomolecule.

77. **(Canceled)**

78. **(Currently Amended)** The adzyme of claim 5 [[37]], wherein said adzyme alters the interaction of said biomolecule with other molecules *in vivo*.

79-106. **(Canceled)**

107. **(Previously Presented)** The adzyme of claim 5, wherein the targeting domain is an antibody or polypeptide(s) including an antigen binding site thereof.

108. **(Previously Presented)** The adzyme of claim 107, wherein the targeting domain is selected from the group consisting of a monoclonal antibody, an Fab and $F(ab)_2$, an scFv, a heavy chain variable region and a light chain variable region.

109. **(Canceled)**

110. (**Withdrawn**) The adzyme of claim 5, wherein said targeting domain is an artificial protein or peptide sequence engineered to bind to said substrate.

111-116. (**Canceled**)

117. (**Currently Amended**) The adzyme of claim 5 [[115]], wherein the protease is selected from among: MT1-MMP; MMP12; tryptase; MT2-MMP; elastase; MMP7; chymotrypsin; and trypsin.

118-126. (**Canceled**)

127. (**Previously Presented**) An adzyme preparation for therapeutic use in a human patient, the preparation comprising an adzyme of claim 5.

128. (**Original**) The adzyme preparation of claim 127, further comprising a pharmaceutically effective carrier.

129. (**Original**) The adzyme preparation of claim 127, wherein the adzyme preparation is formulated such that autocatalytic modification of the adzyme is inhibited.

130. (**Canceled**)

131. (**Currently Amended**) The adzyme preparation of claim 127 [[130]], further comprising a reversible inhibitor of said protease.

132. (**Original**) The adzyme preparation of claim 131, wherein the reversible inhibitor is safe for administration to a human patient.

133. (**Original**) The adzyme preparation of claim 127, wherein said adzyme preparation is substantially pyrogen free.

134. (**Original**) The adzyme preparation of claim 127, wherein said adzyme preparation is packaged with instructions for administration to a patient.

135. (**Withdrawn**) A method of making a medicament for use in treating a disorder that is associated with an activity of the substrate of an adzyme of claim 5, the method comprising formulating the adzyme for administration to a human patient.

136. (**Canceled**)

137. (**Withdrawn**) A method of treating a disorder that is associated with an activity of the substrate of an adzyme of claim 5, the method comprising administering a therapeutically effective dose of the adzyme to a human patient in need thereof.

138-146. (**Canceled**)

147. (**Withdrawn**) A method for manufacturing an adzyme, the method comprising

a) culturing a cell comprising an expression vector comprising a nucleic acid encoding the adzyme of claim 5, in conditions that cause the cell to produce the adzyme; and

b) purifying the adzyme to substantial purity.

148-149. (**Canceled**)

150. (**Withdrawn**) The method of claim 147, wherein the purifying the adzyme to substantial purity includes the use of a reversible inhibitor that inhibits autocatalytic activity of the catalytic domain.

151-155. (**Canceled**)

156. (**Currently Amended**) The adzyme of claim 5 [[1]], wherein the targeting moiety comprises a polypeptide or polypeptide complex.

157. (**New**) The adzyme of claim 5, wherein the adzyme is resistant to autocatalysis.